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SYSTEMS FOR PREPARING FINE PARTICLES AND OTHER SUBSTANCES

FIELD OF INVENTION

This invention relates to controlled preparation of particles with at least one solvent at near or supercritical conditions. It provides methods, measures, apparatus and products produced by the methods. In other aspects, the invention relates to further treatment of formed particles such as encapsulation of formed primary particles, and methods and measures for collection of formed substances in a batch wise or continuous manner. In a further aspect, the invention relates to methods and measures, for producing microemulsions for e.g. the production of fine particles. In a still further aspect, the invention relates to improved methods of controlling chemical reactions in general.

BACKGROUND

There are an increasing interest in nano- and microsized particulate materials in numerous technical applications. Such nanoparticular materials exhibit properties, which are significantly different than those of the same material of larger size. Examples of physical properties, which decreases with decreasing particulate size are: Elastic modulus, density, thermal conductivity etc., whereas physical properties such as strengths, hardness, toughness, ductility, diffusivity, thermal expansion coefficient, solubility etc. increases as a result of size reduction of particular materials. The novel properties of such nanostructured materials can be exploited and numerous new applications developed by using them in different industries. Examples of potential applications include new materials such as improved thermoelectrical materials, electronics, coatings, semiconductors, high temperature superconductors, optical fibres, optical barriers, photographic materials, organic crystals, magnetic materials, shape changing alloys, polymers, conducting polymers, ceramics, catalysts, electronics, paints, coatings, lubricants, pesticides, thin films. composite materials, foods, food additives, antimicrobials, sunscreens, solar cells, cosmetics, drug delivery systems for controlled release and targeting, etc.

Several techniques have been used in the past for the manufacture of micro- or nanoparticles. Conventional techniques include spray drying, freeze drying, milling and fluid grinding, which are capable of producing particles in the micrometer range. A particular high attention is related to techniques operating with solvent(s) at near or supercritical conditions, and in particular under supercritical conditions. Several techniques for particle formation using supercritical fluids have been proposed over the last two decades. They are generally variations of two primary methods for particle precipitation in

supercritical fluids, the Solvent-AntiSolvent technique (SAS) and the Rapid Expansion of Supercritical Solutions technique(RESS).

SAS Technique

In the SAS technique, the material of interest is first dissolved in a suitab'e organic solvent, and the solution is subsequently mixed with a supercritical solvent, which dissolves the solvent and precipitates the solids out as fine particles.

RESS Technique

In the RESS technique, the solid of interest is first solubilized in a supercritical fluid and thereafter expanded by spraying through a nozzle. The expansion through the nozzle causes a dramatic reduction in the CO2 density and thereby a dramatic reduction in the solvent capacity, causing high supersaturation resulting in the formation of fine particles.

Derived techniques from the SAS and RESS techniques are for example Solution Enhanced Dispersion by Supercritical Fluids Techniques(SEDS) and Precipitation with compressed Antisolvent technique (PCA), which is based on the concept of coupling the use of a supercritical fluid as a dispersing agent, by means of a coaxial nozzle, in addition to its primary role as an antisolvent and a vehicle to extract the solvent. Further extensions of this technique includes multi concentric opening nozzles.

Other techniques includes Precipitation from Gas-Saturated Solutions (PGSS), which involves melting the material to be processed, and subsequently dissolving a supercritical fluid under pressure. The saturated solution is then expanded across a nozzle, where the supercritical fluid, which is more volatile escapes leaving dry fine particles.

All these techniques have been succesfully used in small scale to produce microparticles of various materials for numerous applications. Excellent reviews of prior art supercritical partic e formation processes can be found in e.g. Ya-Ping Sun("Supercritical Fluid Technology in Materials Science and Engineering - Syntheses, Properties and Applications, Marcel Dekker Inc., 2002-ISBN: 0-8247-0651-X), Gentile et al (WO03/035673A1), Gupta et al (US2002/0000681A1), Mazen et al (EP0706421B1), Del Re et al (WO02/068107A2), Mazer et al (WO99/44733), Calfors et al, Jagannathan et al (WO03/053561), all of which are hereby included by reference.

However, all these techniques suffer from some inherent limitations. The RESS technique is limited by the solvent capacity in the supercritical fluid. For example, supercritical carbon dioxide, which is a preferred solvent in many applications, is limited by a low solubility towards polar substances. Modifiers such as co-solvents and surfactants may be

added to the supercritical carbon dioxide to improve the solubility of the material of interest. However, such co-solvents and surfactants may remain in the precipitated product as impurities, which may not be acceptable. Further drawbacks of the RESS technique includes that the isenthalpic expansion over the nozzle that results in large temperature drops, which can cause freezing of the solid and carbon dioxide and thereby cause blocking of the nozzle. The nozzle design is further critical for the final particle characteristics such as size and morphology etc. All these drawbacks from microscopic variables limits the control over the process itself, and makes scale up difficult.

Due to the higher solubility the SAS technique and its derivatives generally have higher through puts, and generally produces particles in the range 1-10 micron (Gupta et al, US2002/0000681A1). The key and particle size controlling step of the SAS techniques is the mass transfer rate of the antisolvent into the droplet. Hence, mixing of solution and the supercritical fluid is crucial in order to obtain an intimate and rapid mixing, a dispersion of solution as small droplets into the supercritical fluid is required. Various nozzle designs have been proposed to inject solution and supercritical fluid into a particle formation vessel in order to provide a good mixing. Recent modifications of the SAS technique to reduce the particle size includes atomization techniques such as special designed coaxial nozzles, vibrational atomization, atomization by high frequency sound waves, ultrasonic atomization etc. (US2002000068A1). Though these modified techniques are believed to provide enhanced mass transfer and resulting reduced particle sizes, too rapid particle formation may reduce the control of the size and morphology such as crystallinity of the formed particles, be sensitive to the nozzle design and blockages of the nozzle and be difficult to scale-up.

An objective of the present invention is to provide a an improved method for the formation of fine particles with controlled growth rate, particle morphology and a narrow size distribution, which is less sensitive to drawbacks described in the prior art.

Another objective of the present invention is to provide improved methods and measures for introducing fluid(s), and/or chemical reactant(s) and/or initiator(s)and/or precursor(s) and/or catalyst(s) into a vessel.

A further objective of the present invention to is provide improved methods and measures for controlling a chemical reaction in a dense fluid under near or supercritical conditions.

A still further objective of the present invention is to provide improved methods and measures for coating or encapsulation of formed particles with one or more layers with one or more materials.

A further objective of the present invention is to provide methods and measures for the collection the formed particles in both a batch wise manner and a continuous manner.

DESCRIPTION OF THE INVENTION

The present invention provides a novel way to produce fine particles having a narrow size distribution from a wide range of materials and is in particularly suitable for producing primary particles in the nanometer range such as in the range 1-100 nanometer, such as in the range 1-30 nanometer, and preferable in the range 1-20 nanometer.

Hence, a preferred embodiment of a method according to the present invention comprises

i) introducing one or more substances contained, such as dissolved and/or dispersed in at least one fluid into a vessel by introducing said fluid(s) into the vessel, said vessel containing one or more section(s) comprising a high surface area material,

ii) causing and/or allowing said substances to precipitate at least partly as primary particles on the surface of said high surface area material.

The precipitation is generally caused by change of the solubility of at least one of said substances. The change of said solubility may be performed in a number of ways depending of the specific particle formation application.

One method of changing the solubility involves mixing said fluid(s) containing said dissolved and/or dispersed substances with an antisolvent capable of dissolving at least partly at least one of said fluid(s) and/or a reaction product formed by a chemical reaction occurring as a result of said mixing. The antisolvent may be in a gaseous, liquid or a supercritical state. The antisolvent may be present in the vessel prior to introducing said fluid(s) and/or may be introduced into said vessel together with said high surface area material at one or more points.

Another method of changing the solubility of at least one of said substances, is to expand the fluid(s) containing said substances into the vessel through one or more nozzles such as performed in the Rapid Expansion of Supercritical Solvent (RESS) and the Rapid Expansion of Supercritical solvent into a Liquid (RESOLV) techniques. Still another method involves changing the solubility by changing the temperature of said fluid.

In a preferred embodiment according to the present invention, at least one of said dissolved and/or dispersed substances in said fluid(s) undergoes a chemical reaction. In

such embodiments according to the present invention, it is advantageous to introduce at least one reactant(s) and/or precursor and/or initiator(s) and/or catalyst(s) into the vessel at least partly prior to introducing said fluid(s) containing said substances. It is further advantageous if said high surface area material is capable of adsorbing at least one of said reactant(s) and/or precursor(s) and/or initiators(s) and/or catalyst(s), and preferably in substantially a monolayer. Hereby said reactant can be evenly distributed on said high surface area material thereby resulting in a very controllable reaction and/or particle formation process.

For some applications it is advantageous to introduce said reactant(s) and/or precursor(s) and/or initiator(s) and/or catalyst(s) for said chemical reaction in a stepwise manner. Hence a preferred embodiment according to the present invention comprises steps of

i. introducing into a vessel at least one reactant(s) and/or precursor(s) and/or initiator(s) and/or catalyst(s) for said chemical reaction,

ii. subsequently introducing into a vessel one or more substances dissolved and/or dispersed in at least one fluid.

An aspect of the present invention involves reactive particle formation after the socalled sol-gel route to form e.g. metal oxide(s) and/or a metal hydroxide(s).

Sol-gel synthesis is a traditional method for e.g. making fine ceramic fibers as described in e.g. YA-Ping Sun,"Supercritical Fluid Technology in Materials Science and Engineering – Syntheses, Properties, and Applications", Marcel Dekker, 2002, ISBN:0-8247-0651-X hereby included by reference. It involves forming an aqueous dispersion of oxide particles that is then gelled either by concentrating the dispersion by solvent removal or by carrying out a chemical reaction. For example, one method of sol gel synthesis is to start with a metal alkoxide solution and add a small amount of water to control the hydrolysis and condensation of metal hydroxides. As the sol is dried, these metal hydroxides form a polymeric network through cross linking of the metal oxygen bonds. The method of drying greatly influences the final product morphology. Supercritical drying has been shown to produce soft aggregates that can easily be broken down to a uniform powder. The resulting powder is typically subjected to heat treatment to induce the complete dehydration and crystallisation of oxide particles. Another method of sol-gel synthesis is to start with a solution of a metal salt and a water-soluble polymer. By adding a base to this solution, the metal salt can be converted to metal hydroxides while the polymer cross-links to form a porous network around these metal hydroxides. In this case, the polymer network serves to prevent significant growth and aggregation of the metal hydroxides, so

that it is possible to obtain nanoparticles using this technique. Nanoparticles of a number of ferrites including CoFe2O4, Ni0,5Zn0,5Fe2O4-SiO2, BaFe12O19 and Ge0,5Fe2,5Oy have been prepared using sol-gel synthesis.

Another method of carrying out a sol-gel reaction according to the present invention is to start with an alkoxide precursor dissolved in e.g. supercritical CO2 and/or supercritical ethanol. The metal alkoxide reacts readily with water to produce metal oxides and/or metal hydroxides. Compared with samples made via conventional sol-gel syntheses, supercritical synthesized powders exhibits a higher degree of crystallinity and contains less hydroxide.

In accordance with the present invention, water is first introduced into the vessel so as to saturate the high surface area material. When said supercritical CO2 or mixture of supercritical CO2 is introduced into the vessel the alkoxide precursor reacts with water on the surface of said high surface area to form an oxide and an alcohol. As the water is evenly distributed very fine primary particles having a narrow size distribution are produced on said high surface area material. Another way of controlling the product characteristics according to the present invention is to control the concentration of the alcohol within the vessel in a predefined manner e.g. by withdrawing at least part of the fluid within the vessel at least part of the time to an external recirculation loop, wherein an alcohol and/or other components are added or extracted, and recirculating said fluid to the vessel after condtioning. The alcohol is preferable the same as formed from the reaction, but may also be a different alcohol. Other ways of controlling the particles formed from the reaction according to the present invention includes controlling parameters such as pressure and temperature within the vessel, the type of alkoxide, controlling the reaction time, the characteristics of specific high surface material used, and the ratio of the alkoxide precursor and the water and the alkoxide e.g. by applying the stepwise addition method as described above or the controlled addition via hollow tubular member(s) as further described below.

The time for said particulate forming reaction is generally less than 24 hours, such as less than 12 hours, and preferable less than 8 hours such as less than 4 hours.

The high surface area material applied in a method according to the present invention generally provides a large number of nucleation sites so as to provide a high nucleation rate compared to the particle growth rate, thereby ensuring a fine control of the particles formed.

Typically the high surface area material is arranged in a vessel in one or more section(s) having a porous structure of any shape. The vessel may be whole or partly filled with said high surface area material.

The high surface area material may comprise a wide range of materials depending on the specific application.

In one preferred embodiment the high surface area material may comprise a particulate material. Said particulate material may comprise the same material as one or more of said substances dissolved or dispersed in said fluid(s) introduced into the vessel. In a particular embodiment said high surface area material comprises seed particles which are recycled from a particle collection device, such as a filter such as a membrane filter. In other applications said seed particles comprise a different material, and the particles formed on the surface of said seed particles may be formed so as to provide a coating or encapsulation of said seed particles, e.g. to obtain a controlled release profile.The particulate material may comprise a fixed bed or a fluidised bed. In a preferred embodiment the high surface area material comprises a porous media such as a heterogeneous catalyst support material or a heterogeneous catalyst.

However, in many preferred embodiments said high surface material comprises a fibre material. Depending on the specific application said high surface area material, may be selected in order to provide a specific functionality to the material. One such functionality may be the capability to adsorb specific compounds on the surface, whereby specific properties of the formed particulate product may be controlled. In the specific case, where the application is a reactive particle formation process involving water as a precursor/initiator for the reaction, the material may be selected so as to provide a large adsorption capacity for water, if this is desirable. In such cases a hydrophilic material is selected. If less adsorption of water is desired, a less hydrophilic or even a hydrophobic material may be selected. Nonlimiting examples of high surface area materials suitable for the present invention includes polymers from polypropylene, polyethylene, polystyrene, polyether polymers, polyamide, polyacrylic, polyimide, fluoropolymers, ceramics, and elastomers such as natural, synthetic and cured rubbers, and silicones (siloxane polymers).

Another preferred characteristic of said high surface area material is a high specific area (m2/m3). In general the specific surface area (m2/m3) of said high surface area material is above 500 m2/m3, such as above 1000 m2/m3, such as above 10.000 m2/m3, and preferable above 50.000 m2/m3 such as above 100.000 m2/m3.

The high surface area material may comprise a plurality of fibres. Various ways of arranging such fibres are known in the prior art (e.g. W.S. Winston Ho etal et al, "Membrane Handbook", Van Nordstrand Reinhold, 1992, ISBN 0-442-23747-2, K. Scott,"Handbook of Industrial Membranes", Elsevier Science Publicers, 1995, ISBN 1856172333, Iversen et al, WO95351153, Iversen et al, WO00160095, US690,830, US5,690,823) and are hereby included by reference. Such methods includes random packings, mats, cloths , bundles, twisted bundles, meshs, arrays, etc..

In an aspect of the present invention said fibres comprises a plurality of fibres extending in substantially the same direction. One way of packing such fibres relevant to the present invention is disclosed in US 5,690,823 hereby included by reference.

In the present description with claims the term the term "hollow tubular member(s)" comprises hollow fibres, and other hollow tubular bodies having any cross section, e.g. a hollow tubular chamber. Likewise the term surface of a membrane and similar expressions are intended to mean at least part of a membrane surface.

In general it is advantageous to introduce at least partly one of said fluids into said vessel through the walls of at least one hollow tubular member comprising an inner and an outer surface, and having at least one end communicating with the outside of said vessel. At least part of said hollow tubular member(s) comprising a membrane. Said membrane may comprise a socalled dense membrane. The term dense membrane is known by a man skilled in the art, and is intended to designate membranes having at least one layer being substantially nonporous i.e. having pores of substantially molecular dimensions.

In many embodiments according to the present invention, the membrane(s) is porous. In other applications such membranes are used for filtration of e.g. liquids (nanofiltration, ultrafiltration, microfiltration etc.), and have pores within the range 0,001-100 micron, such as pores in the range in the range 0,01-10 micron, and preferably in the range 0,01-1 micron.

In some embodiments in accordance with the present invention such hollow tubular members are used for introducing at least one of said fluid(s) into the vessel in a very uniform manner. In such embodiments the high surface are may comprise both hollow tubular member(s) and other high surface area materials such as a nonporous fibre material. The hollow tubular member(s) may also comprise several sets of hollow tubular member(s) for introducing different fluids to the vessel. Various examples integrating of said hollow tubular member(s) in the vessel are further illustrated in the figures.

In a particular preferred embodiment for many applications, the hollow tubular member(s) constitutes said high surface area material. In such embodiment a fluid and/or reactant(s) and/or initiator and/or precursor may be added to substantially the outer surface of said tubular member(s).

The present invention is particularly relevant for applications, wherein at least one of said fluids are at near or at supercritical conditions, and in particular applications wherein at least one of the fluids being containing CO2 and/or water and/or an organic solvent and/or an oil. Said fluid(s) may further comprise one or more cosolvents and/or one or more surfactants.

The high surface area material with said deposited primary particles may constitute the final product or be used as template for forming and/or curtailing said particulate material into a specific shape, size and/or structure.

The deposited particulate material may be removed from said high surface area material by applying a vibrating effect and/or an acoustic effect and/or a pulse effect such as a back chock and/or by back flushing with a fluid or by a combination thereof.

Chemical reactions are generally conducted by contacting one or more reactants under appropriate reaction conditions for the reaction to occur. However, many chemical reactions of industrial interest suffer from lack of efficient mixing of the reactants to participate in the chemical reaction, and leads to reduced controllability, and/or reduced selectivity etc.

This method of controlling the addition and distribution of a chemical reactant is believed to be novel per se, and may be applied for other chemical reactions than particle formation processes.

Hence, the present invent further relates to methods, processes, apparatus and products for reacting chemical species in general in a vessel. In a particular embodiment the invention relates to measures and procedures, and apparatus for improving uniformity of chemical reactions, and thereby leading to more controllable and selective reactions. More in particular, the invention relates to chemical reactions, and chemical products produced in a reaction vessel comprising a high surface area material, said high surface area material being capable of adsorbing at least one of the chemical species being introduced into the vessel, and said chemical specie being introduced into the vessel at least partly prior to introducing other reactants for said chemical reaction.

DESCRIPTION OF THE DRAWINGS

Fig.1 shows an example of a vessel containing a high surface area fibre material according to the present invention. The high surface area material is contained in a vessel having one or more inlets for introducing one or more fluids. The vessel may be horisontally or vertically positioned. A randomly packed fibre material is illustrated in Fig. 1b. Fig. 1c shows a reactant (black triangles) adsorbed to said fibre material. Fig. 1d shows said primary particles formed on the surface of said fibre surface, and Fig. 1e shows the harvesting said deposited particles

Fig.2 shows an example of a vessel similar to the one in Fig. 1, but further comprising a hollow tubular member blocked in one end to distribute said first fluid. It should be understood that the vessel may constitutea plurality of such tubular members.
Fig.3 shows a vessel containing a high surface area material according to the present invention comprising a plurality of fibres extending in substantially the same direction and with both ends communicating with the outside of said vessel. The vessel may have one or more inlets communicating with the outside of said vessel for introducing one or more fluids, and the vessel may further have one or more outlets for withdrawing said fluids and/or said particles formed. It should be understood that in addition to said high surface area material, the vessel may further comprise hollow tubular member(s) with one or both ends communicating with the outside of said vessel.

Fig. 4. illustrates a vessel similar to the one in Fig. 3, but further comprising a plurality of hollow tubular members extending in substantially the same direction and communicating with both an inlet and an outlet plenum. The first fluid is introduced into said inlet plenum and is distributed to the inner surface of said tubular member(s). At least part of said fluid permeating through the membrane walls of said tubular members so as to obtain a controlled addition of said first fluid and/or dissolved substances to fluid on the outer surface of said hollow tubular members, thereby resulting in a precise control of the concentration of said fluid and/or dissolved substances within the vessel. The temperature within the vessel can further be precisely controllled by controlling the flow rate and inlet temerature of said first fluid. This is preferably accomplished by withdrawing in at least part of said particle formation process said first fluid from said outlet plenum to an external re-circulation loop (not shown), wherein flow rate, composition, temperature, and pressure are controlled in a predefined manner before re-circulating it to said inlet plenum for said first fluid. In a preferred embodiment the particles deposited on the outer surface of said hollow tubular members are at least partly removed from said surface by closing the outlet for said first fluid e.g. by closing a valve. Thereby substantially all of said first

fluid permeates said membrane wall and clean the surface by back flushing. If said closing of the valve is very fast a back chock (short pressure pulse is obtained). It is further advantageous if said hollow tubular member is made from an elastic material so it is capable of expanding during said pressure pulse. It should be understood that the vessel may further comprise an additional high surface area material in addition to the hollow tubular members shown on the figure.

Fig. 5 shows an example of superimposed layers of hollow tubular members where two different fluids (A and B) can be conducted through the lumen of the fibres, as indicated, whereas a flow of a third fluid can be passed transversely through the fibres from above, perpendicular to the longitudinal direction of the fibres, as indicated by the vertical arrow.

Fig.6 illustrates a situation similar to the one in Fig. 6, but where a wowen array of hollow membrane fibres is used.

ILLUSTRATIVE EXAMPLE 1

There are several reasons for employing drugs as fine powders in pharmaceutics, such as the need to improve the bioavailability of the drug or the requirement for specific pharmaceutical forms (nasal, opthalmic, injectables, modified release etc.).

ILLUSTRATIVE EXAMPLE 2:

SUPERCRITICAL PRODUCTION OF NANOPARTICLES ACCORDING TO THE CURRENT INVENTION

Supercritical fluids are excellent solvents for reactive particle formation, leading to nano-particle products with very narrow size distribution.

The basis of the reactive particle formation method is a chemical system, in which reactants are soluble in the solvent utilized, while the reaction products are insoluble. An example of such system is metal oxides, formed from reaction between metal alcoholates and water. Due to the insolubility of the product the chemical reaction rapidly produces a supersaturated product solution, and hence precipitation starts to take place in the reaction vessel. The precipitation is initiated at, and grows from, any available nucleation site, i.e. vessel walls or seed particles present in the vessel. Precipitation, and accordingly particle growth, continues until the solution is no longer supersaturated. If a sufficiently high number of nucleation sites are provided in the reaction vessel, precipitation time and thereby particle growth is restricted, and very small particlesin the nano-meter range are

formed. Examples of ways to introduce the nucleation sites to the reaction vessel are addition of seed particles or a high surface area material.

In order to ensure the narrow particle size distribution, precipitation time must be controlled accurately, i.e. super-saturation must be achieved in all parts of the vessel at the same time. Several conditions must be fulfilled to achieve such homogenous super-saturation; the mixing of reactants must be homogenous, the chemical reaction should be relatively fast compared to the precipitation time, and the solvent properties should be carefully controlled to ensure homogenous solubility throughout the vessel. Both reactant mixing and solvent property control are facilitated through the circulation loop of the present invention.

ILLUSTRATIVE EXAMPLE 3

An apparatus according to the invention may include

- Reaction vessel assembly
- Dosing assembly for precursor and chemical reactor
- CO_2 recycle system
- Internal discharge assembly
- External filter and product collection assembly
- CO_2 storage assembly

The reaction vessel may be a vertical or a horizontal vessel. In a preferred embodiment a vertical vessel is used for facilities with a small production capacity and horizontal vessels are preferably used for facilities with large production capacity. In each case vessels may be arranged in parallel for optimal plant configuration as determined by a man skilled in the art.

The reaction vessel may be equipped with one or more sections of high surface area material. The material is preferably arranged in a manner that allows easy cleaning and discharge from the high surface area material of the produced chemical reaction products. Without limiting the scope of the invention the high surface area material may be hanging sheets of high surface area materials, hanging bags of high surface area materials or a honey come structured material. The reaction vessel further contains means for discharging the chemical reaction products from the high surface area material by using ultrasound, sonic horns, mechanical shaking, electrostatic discharge forces or any combination hereof.

The reaction vessel contains in the lower part means for collection and transport of the chemical reaction products. In a preferred embodiment a collection is performed using a mechanical conveyor that transports the formedpartculate product to one end of the reaction vessel, where it is discharged into a pneumatic CO_2 transport system, which transport the products to an external filter and debagging system.

CLAIMS

1. A method of producing a particulate material comprising

introducing one or more substances contained, such as dissolved and/or dispersed in at least one fluid into a vessel by introducing said fluid(s) into the vessel, said vessel containing one or more section(s) comprising a high surface area material,

causing and/or allowing, said substances to precipitate at least partly as primary particles on the surface of said high surface area material.

2. A method according to claim 1, wherein said precipitation is provided/caused by a change in the solubility of at least one of said substances.

3. A method according to claim 2, wherein said change in the solubility is provided/caused by an antisolvent present in the vessel.

4. A method according to claim 3, wherein said antisolvent is in a gaseous, liquid, or supercritical state.

5. A method according to claims 2 or 3, wherein said antisolvent is one of the fluids being introduced to the vessel.

6. A method according to any of the claims 2-5, wherein said change in solubility of at least one of said substances is provided/caused by expanding at least one of said fluids containing at least one of said substances into the vessel.

7. A method according to any of the claims 2-5, wherein said change in solubility is provided/caused by a change in the temperature of said fluid(s).

8. A method according to any of the preceding claims, wherein at least one of said substances undergoes a chemical reaction.

9. A method according to claim 8, wherein at least one reactant(s) and/or precursor(s) and/cr initiator(s) and/or catalyst(s) for said chemical reaction is at least partly introduced to the vessel prior to introduction of said fluid(s) containing said substances.

10. A method according to claim 8 or 9, comprising steps of

i. introducing into the vessel at least one reactant(s) and/or precursor(s) and/or initiator(s) and/or catalyst(s) for said chemical reaction

ii. subsequently introducing into the vessel one or more substances dissolved and/or dispersed in at least one fluid.

11. A method according to any of the claims 8-10, wherein the chemical reaction is a supercritical sol-gel reaction.

12. A method according to any of the claims 9-11, wherein said catalyst is an enzyme(s).

13. A method according to claim 9, wherein said high surface area material is capable of adsorbing at least one of said reactant(s) and/or precursor(s) and/or catalyst(s) on said high surface area material.

14. A method according to claim 12, wherein said reactant(s) and/or precursor(s) and/or catalyst(s) is/are adsorbed substantially in a monolayer of said high surface area material.

15 A method according to any of the preceding claims, wherein the time for particulate forming reaction is less than 24 hours, such as less than 12 hours and preferable less than 8 hours, and even more preferable less than 4 hours.

16. A method according to any of the preceding claims, wherein said high surface area comprises a fibrous material.

17. A method according to any of the preceding claims, wherein said high surface area material has a hydrophilic surface.

18. A method according to any of the claims 1-16, wherein said high surface area material is hydrophobic.

19. A method of method according to any of the claims 16-18, wherein said high surface area material is a polymeric material.

20. A method according to any of the claims 16-18, wherein said high surface area polymeric material is polypropylene.

21. A method according to claim 16, wherein said high surface area fibrous material is an elastic material.

22. A method according to any of the claims 1-15, wherein said high surface area material is a ceramic material.

23. A method according to any of the preceeding claims, wherein the specific surface area (m2/m3) of said high surface area material in said sections is above 500 m2/m3, such as 1000 m2/m3, such as above 10.000 m2/m3, and preferably above 50.000 m2/m3 such as above 100.000 m2/m3.

24. A method according to claim 23, wherein said high surface area material is a filtration medium.

25. A method according to any of the preceding claims, wherein said vessel further comprising at least one hollow tubular member comprising an inner and an outer surface, and having at least one end communicating with the outside of said vessel, at least part of said hollow tubular member(s) comprising a membrane, at least one of the fluids being introduced into the vessel through the membrane.

26. A method according to claim 25, wherein said hollow tubular member(s) is blocked in the one end being inside the vessel.

27. A method according to claim 25, wherein both ends of said hollow tubular member(s) are open and are communicating with the outside of said vessel.

28. A method according to claim 25-27, wherein said membrane contains at least one dense layer (dense membrane).

29. A method according to any of the preceding claims 25-28, wherein said membrane is a porous membrane, preferably being a membrane having pores within a range of 0,001-100 micron, such as a pores in the range 0,01-10 micron, and preferably being a membrane having pores within the range of 0,01-1 micron

30. A method according to the claims 25-29, wherein the inlet end of said hollow tubular member(s) is communicating with an inlet plenum, wherein an antisolvent is introduced, at least part of said antisolvent permeating said membrane surface and providing a controlled and uniform distribution of said antisolvent in said vessel.

31. A method according to claim 25-30, wherein at least one of said fluids containing dissolved substances is introduced into the vessel through said hollow tubular member(s).

32. A method according to any of the claims 30 or 31, wherein at least two fluid streams are introduced into the vessel through two separate sets of hollow tubular member(s) each having an inlet plenum communicating with the outside of the vessel.

33. A method according to any of the preceding claims, wherein the high surface area material comprising hollow tubular members according to the claims 25-32.

34. A method according to claim 33, comprising contacting at least part of the inner surface of said hollow tubular member(s) with a first fluid, and contacting at least part of the outer surface(s) of said hollow tubular member(s) with a second fluid, a least part of said first fluid permeating through at least part the wall(s) of said hollow tubular member(s), and mixes with said second fluid substantially at the outer surface(s) of said hollow tubular member(s)

35. A method according to claim 34, wherein a micro-emulsion of said first fluid in said second fluid is formed.

36. A method according to any of the claims 33-35, wherein one of the fluids is water or contains water.

37. A method according to claim 36, wherein said water or water mixture contains one or more substances preferably being dissolved or dispersed therein.

38. A method according to any of the claims 33-37, wherein one of the fluids is CO_2 or an oil.

39. A method according to any of the claim 38, wherein said fluid further comprises one or more surfactants.

40. A method according to any of the claims 33-39, wherein said microemulsion formed comprises a water core.

41. A method according to claim 40, wherein said water core comprises dissolved and/or dispersed substances.

42. A method according to any of the claims 33-41, wherein diameter of said water core in the emulsions formed is in the range 0,5-15 times the diameter of the pores of the membrane part of said hollow tubular member(s), such as in the range 1-10 times the diameter of the pores of the membrane part of said hollow tubular member(s), and preferably in the range 2-4 the diameter of the pores of the membrane part of said hollow tubular member(s).

43. A method according to any of the claims, 33-41, wherein said high surface area material comprises to separate sets of hollow tubular member(s), both sets of said hollow tubular member(s) comprising an inlet plenum and an outlet plenum communicating with the outside of said vessel, and wherein two different fluids can be contacted with the inner side of said hollow tubular member(s), and where two different emulsion(s) of said fluids in said fluid contacting the outer surface of said hollow tubular member(s) are formed.

44. A method according to any of the claims 33-43, wherein said a reaction is occurring in said microemulsion(s).

45. A method according to any of the claims 33-44, wherein said fluid containing said microemulsion(s) are used to dissolve and/or extract substances outside said vessel.

45. A method according to any of the preceding claims, wherein the method involves at least one solvent at near or at supercritical conditions.

46. A method according to claim 45, wherein one of the fluids is CO2.

47. A method according to claim 45, wherein one of the fluids is and organic solvent.

48. A method according to claim 45, wherein one of the fluids is water.

49. A method according to any of the preceding claims, wherein the pressure of at least one of said fluids is in the range 85-500 bar, preferably in the range 85-500 bar, such as in the range 100-300 bar.

50. A method according to any of the preceding claims, wherein the temperature in the vessel is maintained in the range 20-500 °C, such as 30-450 °C, and preferably in the range 35-200 °C, and more preferable in the range 40-150 °C.

51. A method according to any of the preceding claims, wherein at least one of the least one fluid contains at least one cosolvent.

52. A method according to claim 51, wherein the cosolvent is selected from the group consisting of alcohol(s), water, ethane, ethylene, propane, butane, sulfurhexafluoride, nitrous oxide, chlorotrifluoromethane, monofluoromethane, methanol, ethanol, DMSO, isopropanol, acetone, THF, acetic acid, ethyleneglycol, polyethyleneglycol, N,N-dimethylaniline etc. and mixtures thereoff.

53. A method according to any of the preceding claims, wherein at least one of the at least one fluid(s) further comprises one or more surfactants, said surfactants being preferably selected from the group consisting of hydrocarbons and fluorocarbons preferably having a hydrophilic/lipophilic balance value of less than 15, where the HLB value is determined according to the following formula: HLB = 7 + sum(hydrophilic group numbers)-sum(lipophilic group numbers).

54. A method according to any of the preceding claims, wherein said vessel is operating at a substantially constant pressure, such as operating continuously at a constant pressure.

55. A method according to any of the preceding claims, wherein said vessel is operating at substantially constant pressure at more than one pressure level.

56 A method according to any of the preceding claims, comprising re-circulating in at least part time during execution of the method at least part of a fluid or fluid mixture present in the vessel, the re-circulating comprising:

- withdrawing from the vessel at least a part of a fluid from the vessel and feeding it to a re-circulation loop and subsequently feeding the fluid back to the vessel.

57. A method according to claim 56, further comprising the step of controlling the temperature of the fluid in the re-circulation loop.

58. A method according to claim 56 or 57, wherein heat is added and/or extracted from the fluid in the re-circulation loop.

59. A method according to any of the claims 56-58, wherein one or more reactants are added or extracted from the fluid in the recirculation loop.

60. A method according to 59, wherein at least one of the reactants is alcohol and/or water.

61 A method according to any of the preceding claims, wherein the method comprises controlling the temperature-, pressure- and/or density profiles within the vessel.

62 A method according to any of the preceding claims, wherein the temperature profile within the vessel is controlled by controlling the temperature and flow rate of at least one fluid flowing inside said hollow tubular members.

63. A method according to any of the preceding claims, wherein said high surface area material with said precipitated particles thereon comprises the final product.

64. A method according to any of the preceding claims, wherein said high surface area material is a template for forming said particulate material into a specific shape, size and/or structure.

65. A method according to any of the preceding claims, wherein at said particles are removed from said high surface area material by introducing a vibrating effect and/or an acoustic effect such as ultrasound waves and/or by back flushing and/or by applying an pressure pulse effect.

66. A method according to claim 65, wherein said vibrating effect is generated by piezoelectric means.

67. A method according to claim 65, wherein said vibrating effect is generated by a magnetorestrictive means.

68. A method according to any of the preceding claims, wherein said particles are removed from said high surface area material while said high surface area is within the vessel.

69. A method according to any of the claims 68, wherein said removal of said particles are performed according to a back flush or back pulse or a back chock technique.

70. A method according to any of the preceding claims, wherein said removed particles are withdrawn from the vessel by flushing with a fluid or fluid mixture present in the vessel.

71. A method according to claim 72, wherein said fluid containing said formed particulate is fed into a second vessel containing a liquid.

72. A method according to claim 71, wherein said fluid containing said formed particulate material is expanded into said liquid thereby providing said formed particulate material as a dispersion in said liquid.

73. A method according to claim 70, wherein said fluid containing said formed particulate is fed to a bag filter or ceramic filter for separation of said formed particulate material from the fluid.

74. A method according to claim 70, wherein said fluid containing said formed particulate material is fed to a membrane separation device.

75. A method according to claim 70, wherein said fluid containing said formed particulate material is deposited on to a second solid in a second vessel.

76. A method according to claim 75, wherein said deposition is performed by spraying.

77. A method according to any of the preceding claims, wherein said precipitated primary particles on said high surface area material are exposed to one or more coating or encapsulation steps and/or reaction steps with one or more materials.

78. A method according to claim 77, wherein said coating or encapsulation step(s) is performed within the vessel.

79. A method according to any of the claims 77-78, wherein said coating or encapsulation step(s) is performed at least partly during harvesting/removing said particles from said high surface area material.

80. A method according any of the claims 77-79, wherein said coating or a further coating is performed in a second vessel.

81. A method according to any of the preceding claims, wherein said particle producing process is selected among the following particle producing processes: RESS (rapid expansion of supercritical solutions), GAS (Gas Antisolvent), SAS (solvent Anti Solvent), SEDS (Solution Enhanced Dispersion by supercritical fluid), PCA (Precipitation with Compressed Antisolvent), PGSS (Precipitation from Gas-saturated Solutions) and variations thereoff.

82. A method according to any of the preceding claims, wherein additional nucleation sites in the vessel is provided by addition of seed particles.

83. A method according to claim 82, wherein said high surface area constitutes said seed particles.

84. A method according to any of the preceding claims, wherein the number of nucleation sites is further increased by introducing an ultrasound or a vibrating surface effect.

85. A method according to any of the preceding claims, wherein the particles produced are in the nanometer range, such as 1-100 nanometer, preferably smaller than 30 nanometer, preferably smaller 20 nanometer, and evenmore preferably smaller than 10 nanometer.

86. A method according to any of the preceding claims, wherein said particles comprises oxide(s) such as metal oxide(s).

87. A method according to claim 86, wherein said oxides is selected among silica, alumina, zirconia, titania.

88. A method according to claim 86, wherein said oxides is a thermoelectrical material.

89. A method according to claim 88, wherein said thermoelectrical material comprises Bi2Te3 or Bi2Te3 doped with semimetals and/or metals.

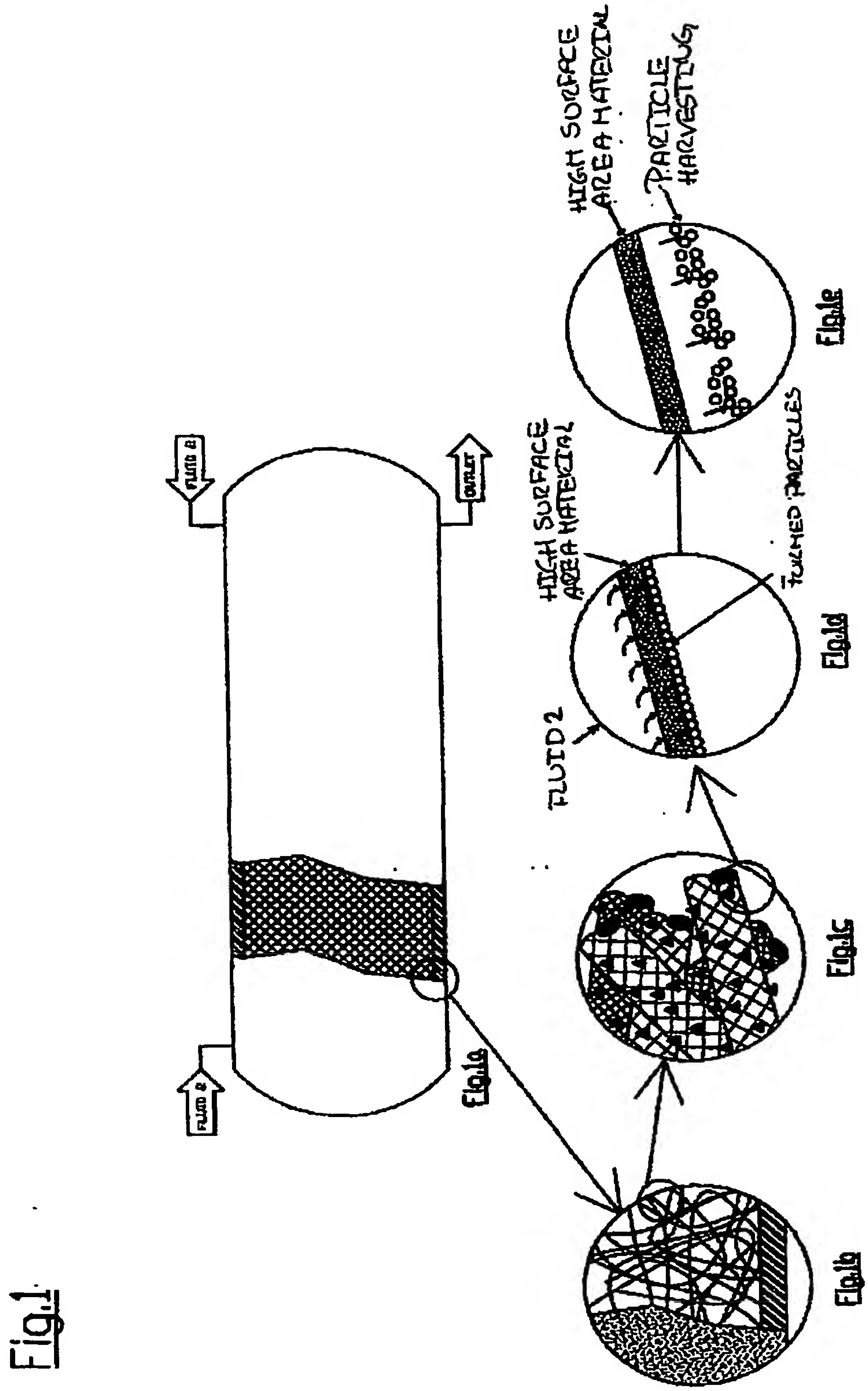
90. A method according to any of the claims 1-85, wherein said particles comprising carbide(s) or nitride(s).

90. A method according to any of the claims 1-85, wherein said particles comprising one or more pharmaceutical and/or biological material.

91. A method according to any of the preceding claims, wherein the material produced is not a particulate material, but in a gas or liquid form

92. An apparatus comprises one or more of the means disclosed in any of the preceding claims and being adapted to carry out the method according to any of the preceding claims.

93 A process comprising steps according to a method of any of the preceding claims.


HIGH SURFACE AREA MATERIAL
PARTICLE HARVESTING
HIGH SURFACE AREA MATERIAL
FLUID 2
Fig.1a
Fig.1b
Fig.1c
Fig.1d
Fig.1e
Fig.1

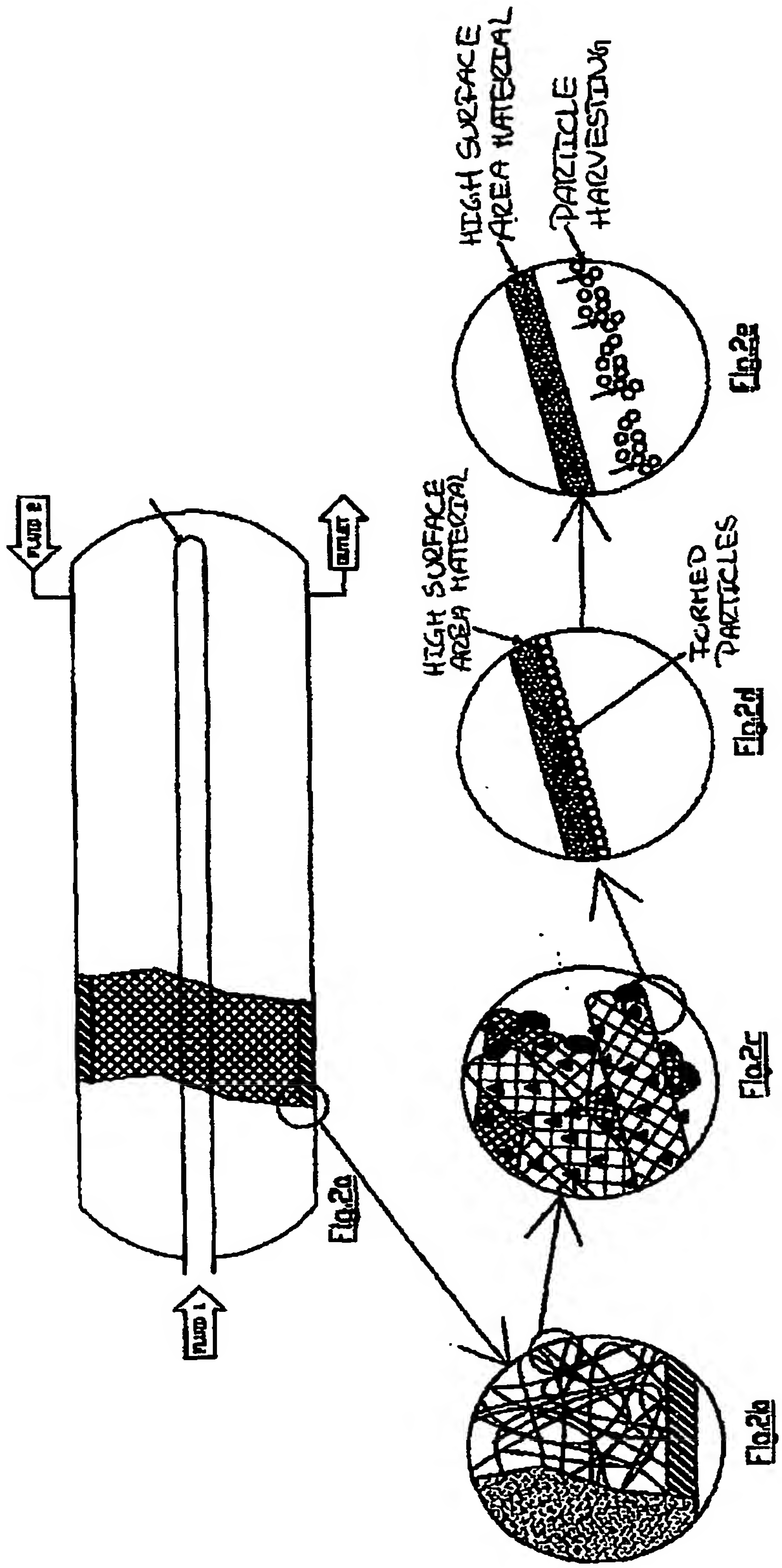

FLUID 2
OUTLET
FLUID 1
Fig.2a
Fig.2b
Fig.2c
HIGH SURFACE AREA MATERIAL
FORMED PARTICLES
Fig.2d
HIGH SURFACE AREA MATERIAL
PARTICLE HARVESTING
Fig.2e

Fig.2

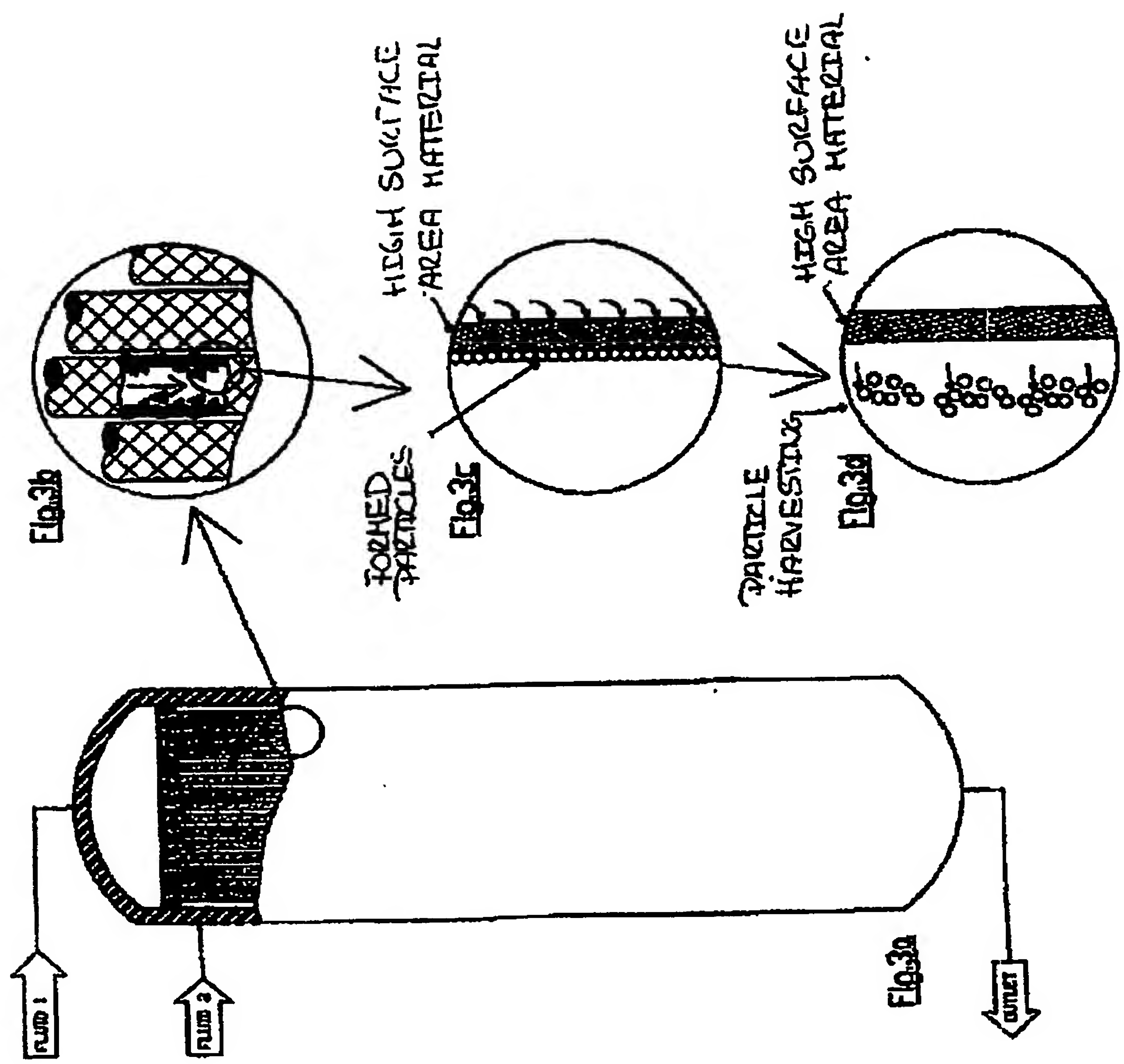

HIGH SURFACE AREA MATERIAL
FORMED PARTICLES
Fig.3b
Fig.3c
HIGH SURFACE AREA MATERIAL
PARTICLE HARVESTING
Fig.3d
Fig.3a
FLUID 1
FLUID 2
OUTLET

Fig.3

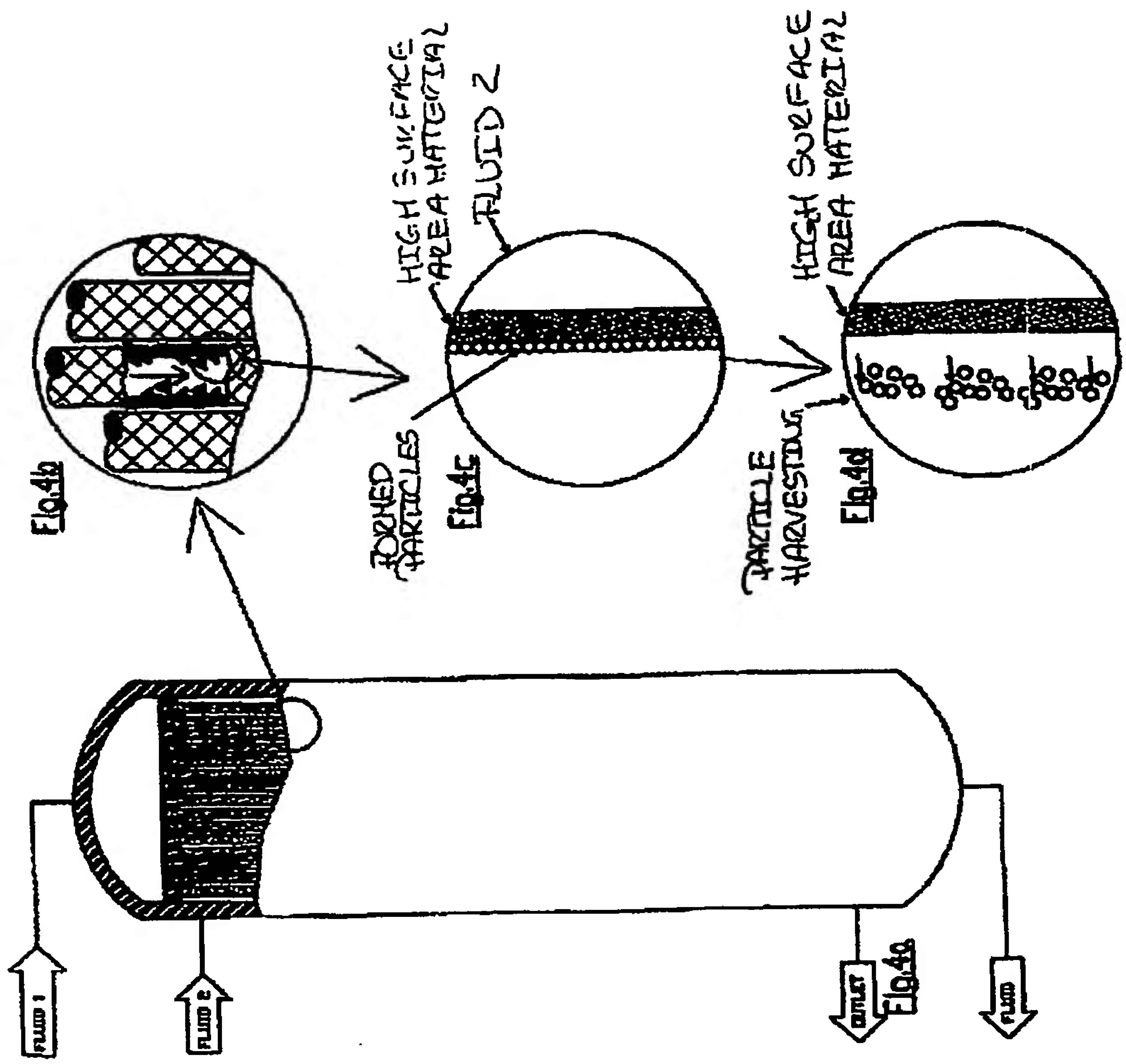

HIGH SURFACE AREA MATERIAL
FLUID 2
FORMED PARTICLES
Fig.4b
Fig.4c
HIGH SURFACE AREA MATERIAL
PARTICLE HARVESTING
Fig.4d
Fig.4a
OUTLET

Fig.4

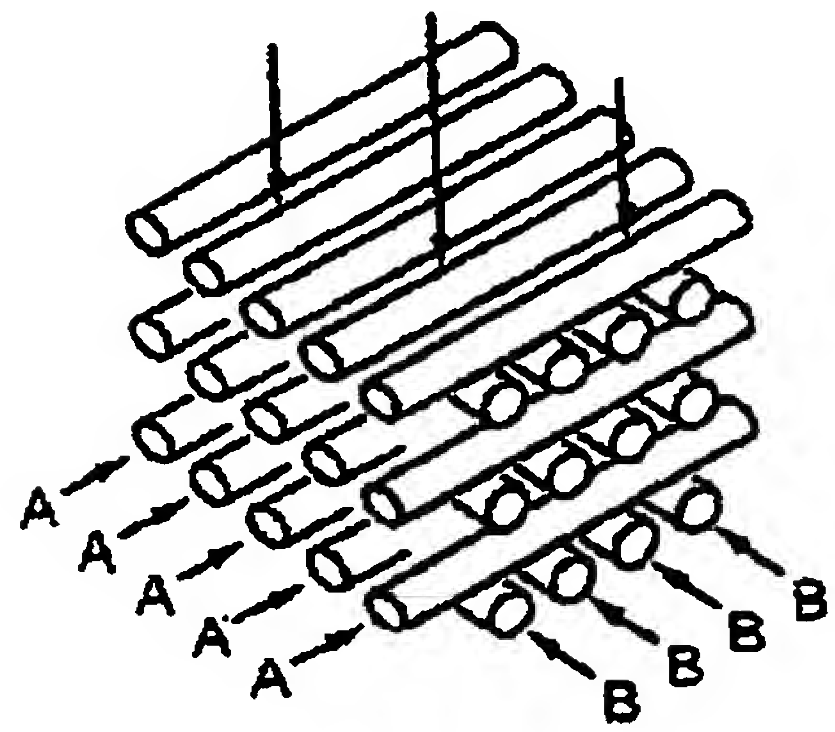


FIG. 5

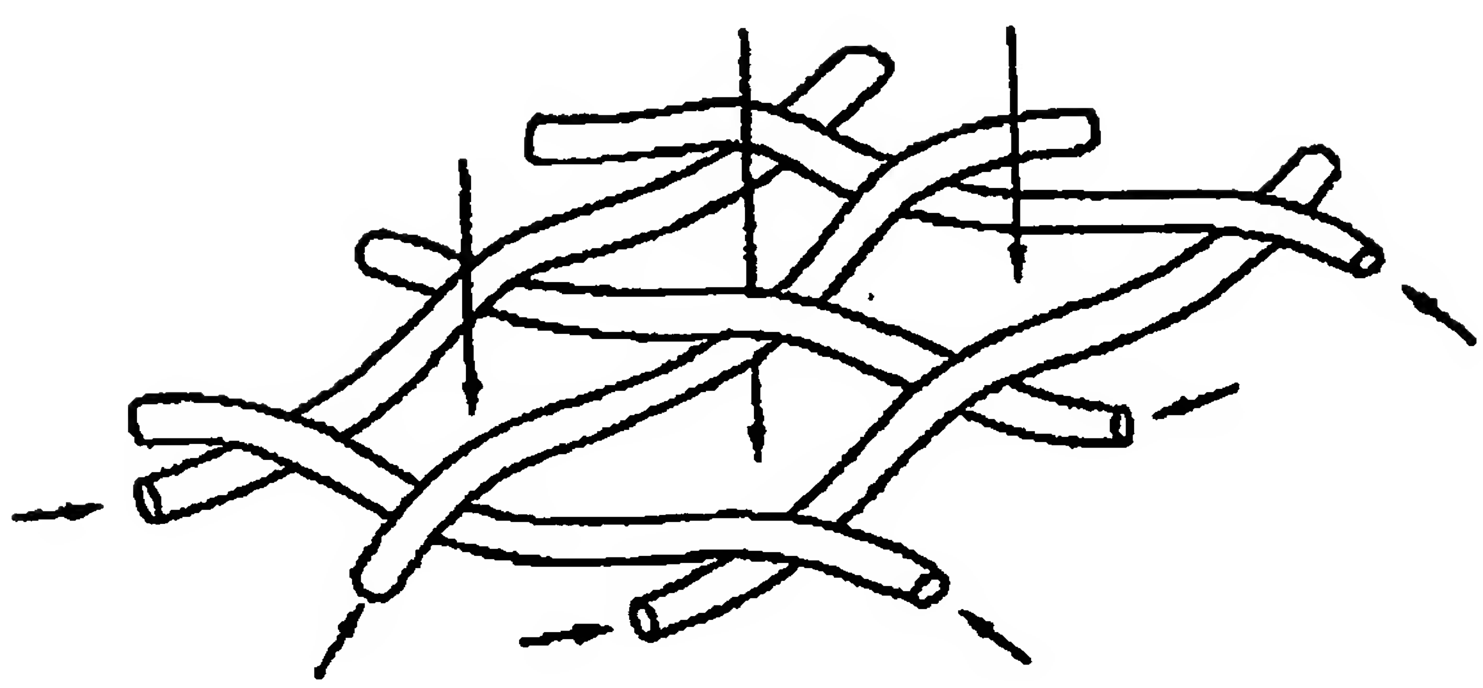


FIG. 6

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